

the art. Simply put, the reagent is the combination of a monoamine, diamide, thiol-containing metal chelator and a targeting moiety covalently linked thereto.

Applicants believe that all grounds of rejection have been traversed by their arguments presented herein. Applicants therefore respectfully submit that all requirements for patentability have been met, and respectfully request that these Claims be brought to issue.

**2. The Claims are non-obvious over the cited prior art.**

The pending claims are asserted to be obvious under 35 U.S.C. §103 over two cited prior art references, taken in combination: Fritzberg *et al.*, U.S. Patent 4,965,392 (the Fritzberg patent); and Rhodes *et al.*, International Application No. WO93/12819 (the Rhodes reference). Applicants respectfully traverse this ground of rejection as follows.

The Rhodes reference, as a published International patent application, has an effective date as prior art under 35 U.S.C. §102(a) on its publication date, July 8, 1993. Applicants submit herewith a Declaration by the named inventors of this application, attesting to the fact that the invention disclosed and claimed herein was invented by them prior to July 8, 1993. Thus, the Rhodes reference is not properly considered prior art to the claimed invention, and Applicants respectfully request that it be withdrawn from use in support of the asserted obviousness rejection.

(Applicants submit this Declaration in unexecuted form and ask the Examiner to consider the Declaration on the merits, awaiting submission of the Declaration signed by the inventors. Applicants will forward the signed Declaration by facsimile to the Examiner as soon as it becomes available.)

Applicants respectfully contend that the remaining reference, considered alone, does not support the asserted obviousness rejection, and fails to make out a *prima facie* obviousness determination. First, the Fritzberg patent was asserted *in combination with* the Rhodes reference, which is positive evidence that the Patent Office believed *both* references *in combination* were required to assert the obviousness rejection. Elimination of the Rhodes reference thus rebuts the assertion of obviousness. Second, Applicants respectfully contend that the teachings of the Fritzberg patent are limited to proteins, *i.e.*, compounds which fall outside the scope of Class 530,

Subclasss 300+ as noted in the Official Action. Finally, Applicants submit herewith a Declaration of Dr. John Lister-James, Senior Director of Research and Development at Diatide, Inc., the assignee of this application. In his Declaration, Dr. Lister-James avers that he has reviewed the specification and claims of the Fritzberg reference. Dr. Lister-James avers that the teachings of this reference would have been understood by one of ordinary skill in the art in view of the teachings of the specification in its entirety. Specifically, Dr. Lister-James avers that the teachings of column 8, lines 15-17 are relevant: "The chelators are synthesized from tripeptides such as glycylglycylglycine and S-protected active esters of acetic acid." Dr. Lister-James notes that all of the exemplified compounds are triamide-protected thiol chelators consistent with the explicitly disclosed method of preparing them. Dr. Lister-James avers that one of ordinary skill in the art would have understood the disclosure of the Fritzberg reference to teach N<sub>3</sub>S chelators of the triamide-protected thiol class. Dr. Lister-James avers that there are no teachings in the reference on how to make or use monoamine, diamide, thiol-containing chelators as disclosed by the instant inventors. Dr. Lister-James also avers that there are no teachings in the reference that would have placed the worker of ordinary skill in the art with a reasonable expectation of success in making and using monoamine, diamide, thiol-containing chelators as disclosed by the instant specification, and that the reference provides no teachings that would have motivated one of ordinary skill in the art to try such chelators.

(Applicants also submit this Declaration in unexecuted form and ask the Examiner to consider the Declaration on the merits, awaiting submission of the Declaration signed by Dr. Lister-James. Applicants will forward the signed Declaration by facsimile to the Examiner as soon as it becomes available.)

In view of Dr. Lister-James declaration, Applicants respectfully contend that the asserted obviousness rejection is based on a hindsight reconstruction of their invention using their own specification as the framework for fashioning the claimed invention from the cited prior art. Applicants contend that there are a multiplicity of compounds that can be produced *on paper* from the generalized formula disclosed in the Fritzberg reference. As evidenced by Dr. Lister-James' declaration, the reference teaches away from the instant invention by teaching triamide, thiol-

containing chelators, thus explicitly teaching a choice of substituents different from those disclosed by the present invention. What is not found in the reference is any teaching, suggestion or motivation to chose *only* those substituents of the general formula that would produce Applicants' claimed invention. These teachings come *solely* from Applicants' disclosure, and it is respectfully submitted that using Applicants specification to provide this critical teachings in support of the asserted obviousness rejection is improper and rebuts the assertion of obviousness.

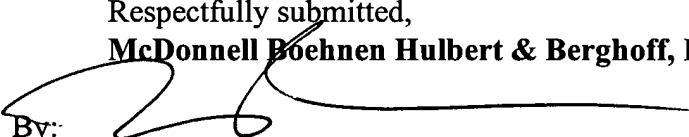
Thus, Applicants respectfully contend that the obviousness rejection has been traversed, and request that it be withdrawn.

### CONCLUSIONS

Applicants believe that all requirements for patentability have been met. They respectfully request that these Claims be brought to issue.

Respectfully submitted,  
**McDonnell Boehnen Hulbert & Berghoff, Ltd.**

By:

  
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